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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,997	06/27/2000	TOSHIO MIYATA	SHIM-004	5507

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,997	MIYATA, TOSHIO	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *9-11,13 and 15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-17* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7-24-00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS's 4-8-03, 11-3-03*.

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-8, 12 and 14 to the extent of SEQ ID NO:2 in the Paper of 11-3-03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 9-11, 13 and 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the Paper of 11-3-03.

Claim Objections

3. Claims 1-8, 12 and 14 are objected to as being directed in part to a non-elected invention, subject matter.of SEQ ID NO's:4 and 6.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification describes a polypeptide sequence consisting of SEQ ID NO:2, which is shown to exhibit increased expression in IgA nephropathy patients in comparison to controls. The peptide is further noted to exhibit activity as a serine protease inhibitor (serpin) protein. However, the claims as written include polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition and which hybridize under stringent conditions, where such stringent conditions are not defined. The instant disclosure of a single polypeptide, that of SEQ ID NO:2 with the instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious,"

and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, the isolated polypeptide sequences of SEQ ID NO: 2 , 4 and 6 and no other amino acid sequences that are proposed to possess the same activity. The similarity appears based solely on homology considerations. Receptor function, however, cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA

93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does allow predictability in this instance. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. The specification and claims fail to set forth a proposed consensus sequence for the genus, and there is no correlation or nexus provided between possession of any structural feature and the encompassed functional features activities such that it is clearly conveyed that possession of any polypeptide having such structural region in common would possess these functional features. Further, even if a proposed consensus sequence were definitive of a genus with a specified function, the instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides and polypeptides encompassed. Thus, the claimed invention lacks adequate written description support.

6. Claims 1-8, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph,

because the specification, while being enabling for the polypeptide and encoding nucleic acids of SEQ ID NO:2, does not reasonably provide enablement for variants of SEQ ID NO:4, 6, sequences replaced, deleted, added and or inserted and functional equivalents or sequences hybridizing to those noted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Applicants claims are directed to peptides with greater than single amino acid substitutions, naturally occurring variants, biologically active peptide fragments and immunogenic fragments as encompassed by the language of "amino acids replaced, deleted, added and/or inserted and functionally equivalent", "hybridizing under stringent conditions".

The specification does not enable the broad scope of the claims which encompasses a multitude of analogs or equivalents because the specification does not teach which residues can or should be modified such that requisite functionality is maintained. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful in any particular use and the skilled artisan would not expect functional conservation amongst homologous

sequences. Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims.

The skilled artisan recognizes that nucleic and amino acid alterations lead to differences in function. For example, the skilled artisan recognizes as noted in Skolnick et al., Trends in Biotech., 18(1):34-39, 2000 and as further exemplified by Choh, PNAS 77(6):3211-14, 1990, that one or more amino acid deletions, insertions or substitutions including truncations results in unpredictable effects in the resulting biological molecule, its' biological function, the ability to bind and/or exhibit similar immunoreactivity. In addition, similar exemplifications are noted in the discussion of related but divergent function of the morphogenic proteins as above. The specification fails to teach the correlation of specific structural and functional activities of the MEGSIN sequences other than the increased expression noted in nephropathy patients and it's apparent membership in the broad class of SERPIN proteins. The specification fails to teach any residues which may be exchanged while retaining requsite activity or function and fail to teach the significance of any variants. As to the nucleic acids, the skilled artisan recognizes that encoding nucleic acids are dependent upon the structural nucleotides and their relationship to the genetic code and translational signals. Further with regard to hybridization, sequences that hybridize are dependent on multiple variables undefined in the claims, in particular G+C content, length, salt concentration and hybridization temperatures, see in particular Sambrook, Molecular Cloning, 1989, 9.47-51 and 11.48-49.

In addition, the specification noted increased mRNA expression in nephropathy patients. However, the specification fails to note such changes in relevant protein expression and fails to distinguish non-cross reactive epitiopes whereby the peptide may be reliably detected. For example, Konopka (Proc. Natl. Acad. Sci. (1986) 83:4049-4052) states that "Protein expression is not related to amplification of the abl gene but to variation in the level of bcr-abl mRNA produced from a single Ph1 template, see in particular abstract.

The specification fails to note suitable epitopes or the relevancy of the peptide data in differential diagnosis of nephropathy patients and the specification fails to teach the variability in the nucleic and peptide sequences that are capable of providing the pertinent function within the full scope of the claim.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed sequences without further undue experimentation.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claims 1-8, and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Tsujimoto et al., US 5,831,030, filed 6-7-1995 and issued 11-3-1998. Prioirity extends to 7-17, 1992.

The Tsujimoto et al., patent teaches polynucleotides and polypeptides of various megakaryocyte differentiation factors comprised of SEQ ID NO:34 bearing 100% similarity to instant SEQ ID NO:2. The patent further discloses the nucleic acid sequence of SEQ ID NO:30 bearing 100% identity with instant SEQ ID NO:1. The patent teaches the nucleic acids in vectors, host cells and methods of producing the polypeptide using recombinant techniques, see in particular columns 2-4. In addition the patent teaches antibodies reactive to the peptide of SEQ ID NO:34 and methods of detection using immunoassay with reactive antibodies, see in particular column 4, 7, and claims. Thus, the reference teachings anticipate the claimed invention.

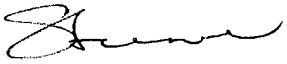
Conclusion

9. No claims are allowed.

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.



Sharon L. Turner, Ph.D.
February 10, 2004